DETAILED ACTION

The Office Action is being re-mailed in order to correct the status of the prosecution by changing the action status from Final to Non-Final. The Examiner inadvertently finalized the rejection. This Action is made NON-FINAL.

This Office Action is in response to the Request for Continued Examination filed December 11, 2007. All previous rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 103 – Obviousness (Previous Rejections)

1) Claims 3-4 and 9-11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Scheiwe et al. (US 6,492,395) in view of Iyer et al. (US 2004/0033257). The rejection is maintained in regards to claims 4 and 9-11 and further applied to claims 1 and 5-8.

Applicant's Arguments

Applicant has amended the claims to limit the compound and solvent to pirfenidone and diethyl glycol monoethyl ether (DGME). Applicant argues Scheiwe discloses that the amount of the active ingredient, i.e., pirfenidone, is preferably within the range of about 0.5% to about 9%. Thus the range taught by Scheiwe et al is not within or close to the presently claimed range. Iyer does not even disclose, teach or suggest a liquid compositions comprising pirfenidone. There is no apparent reason for one of ordinary skill in the art to combine the references with a reasonable expectation of success in achieving the present invention. Even if combined the present invention would not have been achieved since none of the references teach the recited concentration of pirfenidone and DGME as a solvent. The invention also provide unexpectedly superior results due to the combination of pirfenidone and DGME such as good stability; lack of skin irritation and clinical safety. This argument is not persuasive

Examiner's Response

In regards to Applicant assertion that about 0.5% to about 9% is not close to the presently claimed range, which is 10% to 25%, about 9% is close to 10%. Upon further consideration of the reference, the reference discloses a composition was made comprising 10% pirfenidone (See Comparative Example 1). In regards to Iyer, the reference is use to disclose solvents that dissolve poorly soluble compounds. Although pirfenidone is not specifically recited in the reference, it would have been in the relative skill of one of ordinary skill in the art to look to the prior art to identify solvents useful in

dissolving poorly soluble compounds for pharmaceutical use. Therefore there is reasonable expectation of success when combining the two references. In regards to the unexpected results, Applicant does not appear to provide a showing of the unexpected results or pointed out where in the specification unexpected results may be found, therefore it cannot be determined if the results are unexpected.

2) Claims 3-4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Margolin (WO 94/26249) in view of Iyer et al. (US 2004/0033257). The rejection is maintained in regards to claims 4 and further applied to claims 1 and 8.

Applicant's Arguments

Applicant argues Margolin does not specifically disclose, teach or suggest a liquid pharmaceutical composition comprising 10 to 25% pirfenidone and DGME. The reference does not provide examples or a teaching of how to make any of the dosage forms named nor any components or ingredients to make such preparations. The reference does not recognize the problems associated with obtaining a liquid composition having a high concentration of pirfenidone with the presently recited range. Thus Margolin is not enabling for one of ordinary skill in the art to make or use a liquid compositions comprising pirfenidone within the presently claimed range. See Applicant's arguments in regards to Iyer above. Applicant has also submitted a Declaration by Dr. Pyare Seth.

The Declaration of Dr. Seth asserts the disclosure of Margolin is not enabling to make and/or used a "liquid composition" comprising pirfenidone, much less a liquid comprising pirfenidone ranging from 10 to 25%. Margolin list dosage forms but provides no examples of liquid preparation. The two examples do not contain either any composition or any method of their preparation which may be reproducible by any person of ordinary skill in the art. The examples are misleading. Example 1, the capsule would not be expected to show any therapeutic effect because it does not comprise excipients for drug delivery. In regards to Example 2, there is no composition or method of preparation of a hydrophilic cream. It would not be possible to make a high concentration cream as disclosed by the instant claims because the drug must be soluble in water. This assertion is supported by Remington's Pharmaceutical Sciences book. If any other organic liquid is used in place of or together with water, it must not be an irritant and it must be otherwise permissible and or a pharmaceutical quality and also have a good stability to permit incorporation of 5 to 10% of a drug like pirfenidone. Moreover such a solvent should not dissolve the emulgator and other constituents of the emulsion. As such the description of Margolin is not a sufficient teaching or guidance for one of ordinary skill in the art to make a hydrophilic cream containing 5 to 10% of pirfenidone, much less 10 to 25%. The highest possible concentration of the active ingredient reportedly dissolved is 7% without recrystallization. Other attempts to dissolve higher concentrations of pirfenidone have failed and the solvents used irritate the mucous membrane resulting in open wounds and pain, which is unacceptable. The instant invention is a useful and novel innovation to provide a "universal dosage form"

for this important “orphan drug”- Pirfenidone. The declaration is insufficient to overcome the rejection.

Examiner’s Response

The reference does not have to provide examples of how to make each dosage form in order to be enabling. Margolin discloses the amount of pirfenidone to be 1% to 20%, therefore teaching and suggesting a liquid compositions comprising pirfenidone in a range from 10% to 25%. It would also have been in the relative skill of one of ordinary skill in the art to look to prior art such as Iyer to determine which solvent would be suitable to make the recited liquid dosage forms Iyer. Especially in view of the disclosure by Iyer et al. which disclose “Transcutol P is purified diethylene glycol monoethyl ether that acts as a powerful solubilizer for several poorly soluble drugs. It is soluble in water, ethanol, hexylene glycol and propylene glycol, and partially soluble in vegetable oils. It also acts as a co-surfactant in the formulation” (paragraph 0024). It would have been obvious to use it to make more concentrated pharmaceutical solutions of other poorly soluble drugs.

In regards to the Declaration, Applicant has not provided objective evidence to support the assertions of the problems of solubilizing pirfenidone or other assertions made in the Declaration other than Remington's Pharmaceutical Sciences book. Although the examples disclosed do not provide a method of making the compositions, one of skill in the art would be able to look to resources such as Remington's

Pharmaceutical Sciences book (as suggested by the Declaration when it was used by Applicant to show how hydrophilic creams are made) to make the disclosed dosages. In regards to the capsule, this is not a liquid dosage form and therefore is not relied on by the rejection. Even if it were, one of ordinary skill in the art would recognize the need for excipients and therefore would find a suitable excipient to make the capsules of Margolin (as pointed out in the Declaration). In regards to Example 2, one would look to the art to determine suitable co-solvents in the event that the drug of choice, at the desired concentration, was poorly soluble in water, as in the case of pirfenidone. One would only need to find a suitable co-solvent to make the creams for the desired area of application such as the skin in one of the cases of Margolin. The description is sufficient enough to make compositions containing 5 to 10% of pirfenidone, especially in view that the active ingredient has been reportedly dissolved at concentrations up to 7% (as disclosed by Applicant's Declaration). One would only need to find a suitable co-solvent to make compositions of higher concentrations. The compositions of Margolin may be used for topical skin application (see claim 16) and therefore would not irritate the mucous membrane because the mucous membrane would not be contacted by the compositions. Therefore the rejection is maintained.

Claims 1 and 4-11 are rejected.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LEZAH W. ROBERTS whose telephone number is (571)272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. W. R./
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612